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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
10/024,933	12/18/2001	Olga Bandman	PF-0352-2 DIV	4096

27904 7590 05/16/2003

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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/024,933	BANDMAN ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *14-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-20 are at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group IV, Claims 14-16 in Paper No. 6, is acknowledged. The traversal is on the ground(s) that the invention encompassed by the claims of Group II drawn to polynucleotides could be examined at the same time as the invention encompassed by the claims of Group IV without undue burden on the Examiner. Applicants submit that a search of the prior art to determine the novelty of the methods of Group IV would provide information regarding the novelty of the polynucleotides of Group II. Applicants further traverse on the grounds that the Examiner could also examine the claims of Group II without undue burden, in view of the fact that they are related to, although of different scope from, claims already allowed in ancestor application U.S. Patent No. 5,876,996. Applicants argument is not found persuasive because while applicants contend that a search of the polynucleotide invention encompassed by the claims of Group II would overlap with a search of the invention encompassed by the claims of elected Group IV, the are not coextensive. For example, a search of Group II would require search of subclasses 435/253.3 and 435/320.1. A search of each of these subclasses would be unnecessary for the search of the elected group IV. With respect to applicants argument that the claims of group II Could be examined without an undue burden because they are related to, although different in scope, to the claims in the parent application which issued as U.S. Patent

No. 5,876,996, applicant is reminded that as pointed out by applicants, these are different applications and the claims, while related are different in scope and, as such the burden of the necessary new search is not lessened as a result of the issuance of the parent application.

Further, applicants is reminded that the examiner that prosecuted the parent application is not the same as the examiner that is currently prosecuting this instant application.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-13 and 17-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 6.

Priority

Applicants statement on the first line of the specification to state that this application is a divisional application of U.S. application serial number 09/149,534, filed September 8, 1998, which is a divisional application of U.S. application serial number 08/900,565, filed July, 25, 1997 now U.S. Patent No. 5,876,996, issued March 2, 1999, both entitled HUMAN S-ADENOSYL-L-METHIONINE METHYLTRANSFERASE, all of which applications and patents are hereby incorporated herein by reference, is acknowledged. It is noted that U.S. application serial number has issued as U.S. Patent No. 6,379,722 on April 30, 2002. It is suggested that the specification be amended to reflect this information.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of the information disclosure filed 12/18/2001 is acknowledged. Those references considered have been initialed.

Claim Objections

Claims 14-16 are objected to because of the following informalities:

Claims 14-16 each depend from non-elected claim 12.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14 and 15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 14 (15 dependent on) is indefinite in the recitation of "specifically hybridizes" as the specification does not define what constitutes "specifically hybridizes". There is nothing to suggest "which probes" "specifically hybridize" to said target polynucleotide(s) and those conditions under which this "specific hybridization" takes place. Thus there is nothing to suggest what is included within the scope of this term and in the art what is considered "specifically hybridizes" varies widely depending on the individual situation as well as the person making the determination. As such the scope of the claimed methods are unclear with respect to this phrase.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 14-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 14-16 are directed to all possible methods for detecting any target polynucleotide of claim 12 in a sample, comprising hybridizing the sample with a probe comprising at least 20 contiguous nucleotides complementary to said target polynucleotide under conditions whereby a hybridization complex is formed between said probe and said target polynucleotide (claims 14 and 15) or amplifying said target polynucleotide using the polymerase chain reaction (claim 16) and detecting the

presence or absence of said hybridization complex. There is no disclosure of any particular structure to function/activity relationship in the single disclosed target polynucleotide (i.e. SEQ ID NO: 2). The specification only provides the representative methods encompassed by the claims in which the target polynucleotide comprises SEQ ID NO: 2 which encodes a methyltransferase polypeptide, encompassed by these claims. The specification also fails to describe additional representative species of target polynucleotides and thus the claimed methods. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 14-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the claimed hybridization and amplification methods of detection of a target polynucleotide, using a polynucleotide consisting of SEQ ID NO: 2 and fragments thereof as a hybridization probe or an amplification primer, wherein the target polynucleotide comprises SEQ ID NO: 2 which encodes a methyltransferase, does not reasonably provide enablement for any hybridization or amplification method of detection of a target polynucleotide, using any polynucleotide

comprising at least 20 contiguous nucleotides complementary to said target polynucleotide as a hybridization probe or any amplification primer, wherein the target polynucleotide comprises a naturally occurring sequence at least 90% identical to SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 14-16 are so broad as to encompass any hybridization (claims 14 and 15) or amplification (claim 16) method of detection of any target polynucleotide, using any polynucleotide comprising at least 20 contiguous nucleotides complementary to said target polynucleotide as a hybridization probe or any amplification primer, wherein the target polynucleotide comprises any naturally occurring sequence at least 90% identical to SEQ ID NO: 2. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of target polynucleotides detected by the claimed methods, encompassed by the claims, including detection of any target polynucleotide merely 90% identical to SEQ ID NO: 2.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to those hybridization and amplification methods of detection of a target polynucleotide, using a polynucleotide consisting of SEQ ID NO: 2 and fragments thereof as a hybridization probe or an amplification primer, wherein the target polynucleotide comprises SEQ ID NO: 2, which encodes a methyltransferase.

Because of the lack of guidance, the extended experimentation that would be required to determine how to make many of the required hybridization probes and primers and how to use most of the detected target polynucleotides it would require undue experimentation for one skilled in the art to arrive at the claimed methods.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any hybridization (claims 14 and 15) or amplification (claim 16) method of detection of any target polynucleotide, using any polynucleotide comprising at least 20 contiguous nucleotides complementary to said target polynucleotide as a hybridization probe or any amplification primer, wherein the target polynucleotide comprises a naturally occurring sequence at least 90% identical to

SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those target polynucleotides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bokar et al. (Journal of Biological chemistry, Vol. 269, No. 26, pages 17697-17704, 1994, See IDS, Ref No. 5) and Hillier et al. (Wash-Merck EST Project, GENBANK Accession Number AA054310, December 1996).

Bokar et al. teach that the widespread presence of m^6A in mRNA from diverse higher eukaryotic species, along with the striking RNA sequence requirements for methylation, suggests that m^6A and the enzyme responsible for its occurrence in RNA may play an important role in mRNA metabolism. Bokar et al. teach the characterization and partial purification of mRNA N^6-adenosine methyltransferase from Hela Cell Nuclei. Bokar et al. further teach that the characterization and cloning of the

genes that encode the individual subunits of this multicomponent enzyme will allow a better understanding of the underlying complexity of this enzymatic activity and the biological function of the post-transcriptional modification it produces.

Hillier et al. (Wash-Merck EST Project, GENBANK Accession Number AA054310, December 1996) disclose a 463 nucleotide human cDNA fragment which encodes a methyltransferase and has a best local similarity score of 98.2% to the complement of SEQ ID NO: 2, between nucleotide 682 and nucleotide 1128.

One of ordinary skill in the art would have been motivated to use the nucleotide sequence information disclosed by Hillier et al. to detect and isolate a full length human methyltransferase cDNA clone, to lead to a better understanding of the underlying complexity of the methylation of nucleic acids as a post-transcriptional modification mechanism. This motivation comes from the art as well as the teachings of Bokar et al. who state "characterization and cloning of the genes that encode the individual subunits of this multicomponent enzyme will allow a better understanding of the underlying complexity of this enzymatic activity and the biological function of the post-transcriptional modification it produces". Further the cloning of the gene(s) encoding will further the understanding of the process of the methylation of nucleic acids by allowing the enzyme responsible for this process to be produced recombinantly. The many advantages of recombinant production of useful proteins are well known within the art as are recombinant methods of obtaining the necessary genes. These advantages include the ability to produce much larger quantities of the protein, being able to produce the protein in more easily handled organisms, reducing the number of steps

necessary for the purification of a protein and producing the protein in a purer form by using an organism that does not include naturally occurring contaminants of the protein.

One of ordinary skill in the art would have been motivated to use any of a number of commonly used techniques to detect and isolate the full length gene(s) such as methods based on hybridization or methods based on polymerase chain reaction amplification. Those methods based on hybridization would involve the use of the cDNA fragment taught by Hillier et al. as a nucleic acid probe, hybridizing a sample with the probe under conditions whereby a hybridization complex is formed between said probe and a target polynucleotide and detecting the presence of said hybridization complex. Those methods based on polymerase chain reaction amplification would involve the use of the cDNA fragment taught by Hillier et al. to design nucleic acid primers for use in a polymerase chain reaction, amplifying a target polynucleotide in a sample using the designed primers and detecting the presence of said amplified target polynucleotide. The reasonable expectation of success comes from the high degree of knowledge in the art with respect to the identification and detection of polynucleotides using both hybridization and polymerase amplification methodologies and the teachings of Bokar et al. and Hillier et al. who teach that human cells have at least one methyltransferase and thus its encoding polynucleotide. Based on the high degree of similarity between the clone taught by Hillier et al. and instantly disclosed SEQ ID NO: 2 (i.e. greater then 98%), each of the above methods of detection would detect a polynucleotide having the sequence of SEQ ID NO: 2 (encompassed by the

polynucleotide of claim 12) and thus the claimed methods are made obvious by Bokar et al. and Hillier et al.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
May 14, 2003